



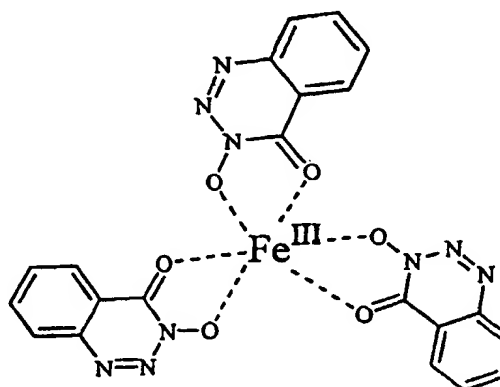
## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>7</sup> : <b>A61N</b>	<b>A2</b>	(11) International Publication Number: <b>WO 00/50117</b>
		(43) International Publication Date: 31 August 2000 (31.08.00)
<p>(21) International Application Number: PCT/US00/04915</p> <p>(22) International Filing Date: 25 February 2000 (25.02.00)</p> <p>(30) Priority Data: 60/122,097 26 February 1999 (26.02.99) US</p> <p>(71) Applicant (for all designated States except US): ADVANCED RESEARCH AND TECHNOLOGY INSTITUTE, INC. [US/US]; Suite 100, 1100 Waterway Boulevard, Indianapolis, IN 46202-2156 (US).</p> <p>(72) Inventor; and (75) Inventor/Applicant (for US only): ZALESKI, Jeffrey, M. [US/US]; 3704 Tamarron Drive, Bloomington, IN 47408 (US).</p> <p>(74) Agents: HASAN, Salim, A. et al.; Leydig, Voit &amp; Mayer, Ltd., Suite 4900, Two Prudential Plaza, 180 North Stetson, Chicago, IL 60601-6780 (US).</p>		<p>(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p><b>Published</b> Without international search report and to be republished upon receipt of that report.</p>

(54) Title: COMPOUNDS, COMPOSITIONS, AND METHODS FOR PHOTODYNAMIC THERAPY

## (57) Abstract

Disclosed are novel compounds, compositions, and methods that are particularly useful in photodynamic therapy. In particular, the inventive compounds, compositions, and methods relate to the formation of cytotoxic radical species in the presence of light. Significantly, the compounds, compositions, and methods of the present invention do not require the presence of oxygen in the photodynamic therapy and, as such, rely on a unimolecular mechanism for producing the radicals. The inventive compounds, compositions, and methods can be used, for example, in the treatment of cancers as well as infections caused by microorganisms such as protozoa, fungi, bacteria, and viruses.



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# PATENT COOPERATION TREATY

## PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

18 APR 2001

WIPO

PCT

Applicant's or agent's file reference 203955	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/04915	International filing date (day/month/year) 25 February 2000 (25.02.2000)	Priority date (day/month/year) 26 February 1999 (26.02.1999)	
International Patent Classification (IPC) or national classification and IPC IPC(7): C07D 487/22; A61K 31/40 and US Cl.: 514/183, 184, 185; 540/145, 450, 456, 460, 461, 470, 472, 474			
Applicant ADVANCED RESEARCH AND TECHNOLOGY INSTITUTE, INC.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 14 September 2000 (14.09.2000)	Date of completion of this report 19 January 2001 (19.01.2001)
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Brenda Coleman Telephone No. 703-308-1235  <b>TERRY J. DEY</b> <b>PARALEGAL SPECIALIST</b> <b>TECHNOLOGY CENTER 1800</b>

Form PCT/IPEA/409 (cover sheet)(July 1998)

**I. Basis of the report**

## 1. With regard to the elements of the international application:\*

- ☒ the international application as originally filed.
- ☒ the description:  
pages 1-63 as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.
- ☒ the claims:  
pages 64-99, as originally filed  
pages NONE, as amended (together with any statement) under Article 19  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.
- ☒ the drawings:  
pages 1-10, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.
- ☐ the sequence listing part of the description:  
pages NONE, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

**IV. Lack of unity of invention**

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.  
☒ paid additional fees.  
☐ paid additional fees under protest.  
☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention is accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.  
☒ not complied with for the following reasons:

Please See Continuation Sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.  
☐ the parts relating to claims Nos. \_\_\_\_\_

**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

International application No.

PCT/US00 5

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. STATEMENT**

Novelty (N)

Claims 1-116 YES  
Claims NONE NO

Inventive Step (IS)

Claims 1-116 YES  
Claims NONE NO

Industrial Applicability (IA)

Claims 1-116 YES  
Claims NONE NO

**2. CITATIONS AND EXPLANATIONS (Rule 70.7)**

Claims 1-116 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the compounds, compositions or method of use of the compounds of the instant invention.

Claims 1-116 meet the criteria set out in PCT Article 33(4), for industrial applicability.

----- NEW CITATIONS -----

NONE

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

**IV. 3. This Authority considers that the requirement of unity of invention is accordance with Rules 13.1, 13.2 and 13.3 is not complied with for the following reasons:**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-7 (in part), 15-19 (in part), 30-36, 52-54, 55 (in part), 60 (in part), 63-72, 76, 79-84, 93, 103 (in part), 105-107 and 110-116, drawn to compounds of formula in claim 1, wherein L is attached to macrocycle and/or polycycle, method of treating cancer using these compounds and pharmaceutical compositions.

Group II, claim(s) 1-7 (in part), 8, 9, 13 (in part), 19 (in part), 20-24, 28, 29, 37, 39, 40, 41 (in part), 42-47, 51, 56-59, 60 (in part), 75, 77, 78, 92, 94-96, 103, 106, 108, 109, 111 and 112, drawn to compounds of formula in claim 1, wherein L is attached to N-containing heterocycle, method of preparation and their compositions.

Group III, claim(s) 1-7 (in part), 15, 16, 17, 19 (in part), 25-29, 49, 50, 60 (in part), 61, 62, 66 (in part), 103 (in part), 113 (in part) and 114-116, drawn to compounds of formula in claim 1, wherein L is attached to aryl group and compositions.

Group IV, claim(s) 1-7 (in part), 10-12, 13 (in part), 14 (in part), 38, 48 (in part), 74 (in part) and 90, drawn to compounds of formula in claim 1, wherein L is attached to phosphorus containing compounds.

Group V, claim(s) 1-7 (in part), 10-12, 13 (in part), 14 (in part), 37 (in part), 38, 48 (in part), 73, 74 (in part), 90, 91, 104 and 105, drawn to compounds of formula in claim 1, wherein L is attached to diyne, method of making and compositions.

Group VI, claim(s) 85-89 and 97-102, drawn to different method, namely, treating infection caused by micro organisms.

The inventions listed as Groups I-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The compounds in groups I-VI are classified in different classes and subclasses. A reference of one will not be a reference to another group. These inventions have acquired different status in the art because of divergent subject matter.

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

HASAN, Salim, A.  
Leydig, Voit & Mayer, Ltd.  
Suite 4900  
Two Prudential Plaza  
180 North Stetson  
Chicago, IL 60601-6780  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 18 September 2001 (18.09.01)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference 203955	
International application No. PCT/US00/04915	International filing date (day/month/year) 25 February 2000 (25.02.00)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input checked="" type="checkbox"/> the inventor	<input type="checkbox"/> the agent <input type="checkbox"/> the common representative
Name and Address	State of Nationality	State of Residence
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	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input type="checkbox"/> the name	<input type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence
Name and Address RAWAT, Diwan, Singh 316 E, Apt. 19, University Bloomington, IN 47101 United States of America	State of Nationality US	State of Residence US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary: <b>Additional applicant/inventor for US only.</b>		
4. A copy of this notification has been sent to:		
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<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer  Marie-José DEVILLARD
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38



## PATENT COOPERATION TREATY

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Name and Address RAWAT, Diwan, Singh 316 E, Apt. 19, University Bloomington, IN 47101 United States of America	State of Nationality US
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## (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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31 August 2000 (31.08.2000)

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(10) International Publication Number  
WO 00/50117 A3

(51) International Patent Classification: C07D 487/22, A61K 31/40

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(22) International Filing Date: 25 February 2000 (25.02.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data: 60/122,097 26 February 1999 (26.02.1999) US

(71) Applicant (for all designated States except US): ADVANCED RESEARCH AND TECHNOLOGY INSTITUTE, INC. [US/US]; Suite 100, 1100 Waterway Boulevard, Indianapolis, IN 46202-2156 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): ZALESKI, Jeffrey, M., [US/US]; 3704 Tamaron Drive, Bloomington, IN 47408 (US).

(74) Agents: HASAN, Salim, A. et al.; Leydig, Voit &amp; Mayer, Ltd., Suite 4900, Two Prudential Plaza, 180 North Stetson, Chicago, IL 60601-6780 (US).

(81) Designated States (national): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— With international search report.

(83) Date of publication of the international search report: 30 November 2000

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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905\*

Applicant please note:

Two inventors listed on Declaration  
and only one on international application.

WO 00/50117 A3

(54) Title: COMPOUNDS, COMPOSITIONS, AND METHODS FOR PHOTODYNAMIC THERAPY

(57) Abstract: Disclosed are novel compounds, compositions, and methods that are particularly useful in photodynamic therapy. In particular, the inventive compounds, compositions, and methods relate to the formation of cytotoxic radical species in the presence of light. Significantly, the compounds, compositions, and methods of the present invention do not require the presence of oxygen in the photodynamic therapy and, as such, rely on a unimolecular mechanism for producing the radicals. The inventive compounds, compositions, and methods can be used, for example, in the treatment of cancers as well as infections caused by microorganisms such as protozoa, fungi, bacteria, and viruses.

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		<input type="checkbox"/> the residence	
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The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35		Authorized officer Marie-José DEVILLARD Telephone No.: (41-22) 338.83.38	

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